Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Betula verrucosa (Itulazax 12 SQ-Bet) for treating moderate to severe allergic rhinitis, conjunctivitis, or both, caused by tree pollen in people 5 to 17 years ID6537

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of itulazax 12 standardised quality pollen from white birch (betula verrucosa) sublingual lyophilisate immunotherapy (12 SQ-Bet SLIT) within its marketing authorisation for treating moderate-to-severe allergic rhinitis, conjunctivitis, or both, induced by pollen from the birch homologous group in people 5 to 17 years old.

Background

Birch pollen allergy is an immunoglobulin E (IgE)-mediated hypersensitive reaction to the pollen of birch trees and related species. When a person with an allergy comes into contact with birch pollen, the immune system recognises it as a threat and produces antibodies. Further contact with the pollen then results in the release of inflammatory substances such as histamine, which leads to the typical allergic symptoms, including rhinitis and conjunctivitis.[1]

Allergic rhinitis is inflammation of the nose that occurs when the nasal mucosa becomes exposed and sensitised to allergens. Depending on the nature of the allergen, allergic rhinitis has traditionally been categorised as either seasonal allergic rhinitis (e.g., induced by pollen) or perennial allergic rhinitis (e.g., induced by animals or dust mites). Rhinitis typically causes symptoms such as sneezing, nasal discharge, itching, and congestion. It may also lead to complications such as sinusitis or middle ear infections as well as the worsening of asthma symptoms.[2]

Allergic conjunctivitis is the inflammation of the conjunctiva, the mucous membranes that line the inside of the eyelids and the sclera, the white part of the eye. Symptoms can include itchy and reddened eyes, swollen conjunctiva and watery discharge, which may be thickened with mucous.[3]

Symptoms of rhinoconjunctivitis (commonly referred to as hay fever) may be intermittent or chronic during the pollen season.[4] Rhinoconjunctivitis can be further categorised as either ‘mild’, ‘moderate’ or ’severe’. The definition of moderate disease from the European Academy of Allergy and Clinical Immunology is that symptoms are “bothersome”. Severe rhinoconjunctivitis occurs when symptoms become hard to tolerate, disrupting daily activities or sleep.[5]

Although allergic rhinitis and allergic conjunctivitis are common conditions, current epidemiological estimates remain imprecise because of a paucity of recent studies, heterogenous terminology and diagnostic criteria, and widespread self-medication practices that contribute to underdiagnosis.[2,3] It is estimated that about 10% of 6 and 7-year-olds and 15% to 19% of 13 and 14-year-olds are affected by allergic rhinitis in England, based on a UK primary healthcare database review (1999–2005).[6] It is

suggested that new cases of seasonal allergic rhinitis increase by a constant rate of around 2% per year between the ages of 3 and 12 years.[2] About 30% to 71% of people with allergic rhinitis may also be affected by allergic conjunctivitis or conjunctival symptoms.[3] The International Study of Asthma and Allergy in Childhood found that in Western Europe, allergic rhinoconjunctivitis in 6 to 7-year olds was estimated to be about 7% and 14% in 13 to 14-year olds.[7]

There is no NICE guidance for treating allergic rhinitis or conjunctivitis or both in people 5 to 17 years old. In practice, initial treatment may involve allergy avoidance. This can be followed by pharmacotherapy aimed at symptom control, which may include antihistamines, ocular mast cell stabilisers, topical nasal corticosteroids, and leukotriene receptor antagonists (if asthma is also present). For severe allergic rhinitis that does not respond to usual pharmacotherapy, specific desensitisation with immunotherapy may be considered.[8] Skin prick or specific IgE tests can be used to establish which allergens trigger the immune response if immunotherapy is being considered.

For adults, NICE technology appraisal guidance 1087 recommends betula verrucosa as an option to treat moderate to severe allergic rhinitis or conjunctivitis caused by pollen from the birch homologous group of trees in people with:

- symptoms despite using symptom-relieving medicines
- a positive sensitisation test (skin prick test or specific immunoglobulin E) to a member of the birch homologous group.

The technology

Itulazax 12 standardised quality pollen from white birch (betula verrucosa) sublingual lyophilisate immunotherapy (12 SQ-Bet SLIT; Itulazax, ALK-Abello) has a marketing authorisation for the treatment of moderate-to-severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group in adults and children (5 years or older). It is indicated in people with a clinical history of symptoms despite use of symptom-relieving medication and a positive test of sensitisation to a member of the birch homologous group (skin prick test and/or specific IgE). Birch homologous group include Betula verrucosa (birch), Alnus glutinosa (alder), Carpinus betulus (hornbeam), Corylus avellana (hazel), Quercus alba (oak) and Fagus sylvatica (beech).

Intervention(s)	Itulazax 12 SQ-Bet SLIT as an add-on to standard therapy
Population(s)	People 5 to 17 years old with moderate-to-severe allergic rhinitis, conjunctivitis, or both, caused by pollen from the birch homologous group despite the use of symptom-relieving medication and a positive test of sensitisation to a member of the birch homologous group (such as a skin prick test or blood test for a specific IgE)
Comparators	Established clinical management without Itulazax 12 SQ-Bet SLIT, such as Pollinex Trees

Outcomes	The outcome measures to be considered include: • combined symptom and medication score • rhinoconjunctivitis symptom scores • complications of allergic rhinoconjuctivitis • medication usage • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. The use of itulazax 12 SQ-Bet SLIT is conditional on a positive test for birch pollen sensitisation confirmed with a skin prick test, radioallergosorbent test, fractional exhaled nitric oxide test or blood test for a specific IgE. The economic modelling should include the costs associated with diagnostic testing for birch pollen sensitisation in people with allergic rhinitis or allergic conjunctivitis who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introductionto-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:**

	Betula verrucosa for treating moderate to severe allergic rhinitis or conjunctivitis caused by tree pollen (2025) NICE technology appraisal guidance 1087. Omalizumab for treating severe persistent allergic asthma (2013) NICE technology appraisal guidance 278. **Related technology appraisals in development:** STG320 for treating allergic rhinitis or rhinoconjunctivitis caused by house dust mites. NICE technology appraisal guidance [ID1278]. Publication date to be confirmed. **Related interventional procedures:** Cryotherapy for chronic rhinitis (2023) NICE interventional procedures guidance 771. Intranasal phototherapy for allergic rhinitis (2018) NICE interventional procedures guidance 616. **Related diagnostics guidance:** ImmunoCAP ISAC 112 for multiplex allergen testing (2016) NICE diagnostics guidance 24. **Related quality standards:** Asthma (2013, updated 2018) NICE quality standard 25.

Questions for consultation

Where do you consider itulazax 12 SQ-Bet SLIT will fit into the existing care pathway for moderate-to-severe allergic rhinitis, conjunctivitis, or rhinoconjunctivitis?

Please select from the following, will 12 SQ-Bet SLIT be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would 12 SQ-Bet SLIT be a candidate for managed access?

Do you consider that the use of 12 SQ-Bet SLIT can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit

and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which 12 SQ-Bet SLIT is licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1.Sheikh A, Panesar SS, Salvilla S, et al. (2009) Hay fever in adolescents and adults. BMJ Clinical Evidence [online]. Accessed August 2025.

2. NHS (2024) Allergic rhinitis. Accessed August 2025.

3. NICE CKS (2022) Conjunctivitis – allergic. Accessed August 2025.

4. University of Worcester (2020) Pollen calendars by area. Accessed August 2025.

5. Pfaar O, Demoly P, Gerth van Wijk R, et al. (2014) Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: An EAACI Position Paper. Allergy 69(7):854-867.

6. Ghouri N, Hippisley-Cox J, Newton J, et al. (2008) Trends in the epidemiology and prescribing of medication for allergic rhinitis in England. Journal of the Royal Society of Medicine 101(9):466-472.

7. Mallol J, Crane J, von Mutius E, et al. (2013) The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: A global synthesis. Allergologia et Immunopathologia 41(2):73-85.

8. Scadding GK, Kariyawasam HH, Scadding G, et al. (2017) BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). Clinical and Experimental Allergy 47(7):856-889.